REMARKS

Applicants thank Examiner Belyavskyi and Supervisory Patent Examiner Chan for the courtesy of the interview on August 1, 2005; for withdrawing the anticipation rejection under 35 U.S.C. § 102(e) with respect to U.S. Patent No. 5,837,460 to Von Feldt *et al.* ("the '460 patent"); and for withdrawing the finality of the previous office action. Claims 29-34 are presently pending and have been examined. Favorable reconsideration and allowance are respectfully requested.

The 102(a) Rejection

Claims 29-33 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated by U.S. Patent Application Publication No. US 2002/0141994 to Devalaraja et al. ("the '994 publication").

Applicants respectfully note that the '994 publication is not a proper § 102(a) reference because its publication date of October 3, 2002 is after both Applicants' U.S. filing date of May 20, 2001 and Applicants' earliest priority date of May 8, 2000 (for U.S. Serial No. 60/202,392). Accordingly, the '994 publication is not a § 102(a) reference to the present application and this rejection should be withdrawn.

Because the '994 publication also appears to be *prima facie* applicable as a reference under § 102(c)(1), Applicants address that possibility herein and establish that the '994 publication is only entitled to an earliest effective filing date of February 23, 2001. Because that date is also after Applicants' earliest effective filing date of May 8, 2000, the '994 publication cannot likewise be applied as a reference under § 102(e)(1) against the present case.

The '994 publication was originally filed as a provisional application on February 23, 2001 and assigned U.S. Serial No. 60/270,948 ("Provisional B"). On July 9, 2001, a petition was filed in that provisional application ("Petition") requesting that it be converted to a non-provisional application. The Petition included a request for priority to an even earlier provisional application filed on March 20, 2000 and assigned U.S. Serial No. 60/190,842 ("Provisional A").[1] Such a priority claim was impermissible. The basis therefore is readily apparent when the chronology below is considered:

March 20, 2000	Provisional A
February 23, 2001	Provisional B
March 21, 2001 -July 8, 2001	No additional filings; Prov. A is thus abandoned
July 9, 2001	Petition to convert Prov. B (with priority claim to Prov. A)

Pursuant to 35 U.S.C. § 111(b)(5),[2] a provisional application becomes abandoned when it is not converted to a non-provisional application within one year of filing,[3] and, once abandoned, that provisional application cannot be revived. Hence, Provisional A became abandoned on March 21, 2001. *Accord*, Paris Convention, Article 4.C.(4).[4] Thus, when Provisional B was

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[1] The evidence establishing the foregoing is provided in Appendix A.

[2] The full text of 35 U.S.C. § 111(b)(5) provides:

(5) Abandonment.--Notwithstanding the absence of a claim, upon timely request and as prescribed by the Director, a provisional application may be treated as an application filed under subsection (a). Subject to section 119(e)(3) of this title, *if no such request is made, the provisional application shall be regarded as abandoned 12 months after the filing date of such application and shall not be subject to revival after such 12-month period. (Emphasis added.)*

[3] Subject to the rule that conversion can be taken on the next available business day. Clearly not at issue here.

[4] This section of the Paris Convention provides:

(4) A subsequent application concerning the same subject as a previous first application within the meaning of paragraph (2), above, filed in the same country of the Union shall be considered as the first application, of which the filing date shall be the starting point of the period of priority, if, at the time of filing the subsequent application, the said previous application has been withdrawn, abandoned, or refused, without having been laid open to public inspection and without leaving any rights outstanding, and if it has not yet served as a basis for claiming a

converted to a non-provisional application, Provisional A was already abandoned and could not be revived. Accordingly, the '994 publication is only entitled to an earliest priority date of Provisional B, namely February 23, 2001.

That this is the case is further confirmed by 37 C.F.R. § 1.53(c)(3) which provides, and actually cautions, that a "provisional application . . . may be converted to a nonprovisional application . . . and accorded the original filing date of the provisional application." Such conversion "will result in the term of any patent to issue from the application being measured from at least the filing date of the provisional application . . . [and] applicants should consider avoiding this adverse patent term impact . . . ."[5] Moreover, it is incontrovertible that had the applicants in the '994 publication done as alternatively suggested in this rule, *i.e.*, file a non-provisional application claiming priority to Provisional B on July 9, 2001 (or on a later date, up to February 23, 2002), no priority claim could have been made to Provisional A because that application was filed 16 (or more) months earlier.

Accordingly, the '994 publication is only entitled to an earliest effective filing of February 23, 2001. Since this date is after Applicants' earliest effective filing date of May 8, 2000, the '994 publication does not constitute a proper reference under § 102(e)(1) and is not available as prior art against the present application.

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right of priority. *The previous application may not thereafter serve as a basis for claiming a right of priority. (Emphasis added.)*

[5] The relevant portions of 37 C.F.R. § 1.53(c)(3) provide

(3) A provisional application filed under paragraph (c) of this section may be converted to a nonprovisional application filed under paragraph (b) of this section and accorded the original filing date of the provisional application. The conversion of a provisional application to a nonprovisional application will not result in either the refund of any fee properly paid in the provisional application or the application of any such fee to the filing fee, or any other fee, for the nonprovisional application. Conversion of a provisional application to a nonprovisional application under this paragraph will result in the term of any patent to issue from the application being measured from at least the filing date of the provisional application for which conversion is requested. Thus, applicants should consider avoiding this adverse patent term impact by filing a nonprovisional application claiming the benefit of the provisional application under 35 U.S.C. 119(e) (rather than converting the provisional application into a nonprovisional application pursuant to this paragraph).

The Three 103(a) Rejections

A. The First 103(a) Rejection

Claims 29-33 have been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by the '460 patent in view of Janeway *et al.* (1999) Immunobiology, p. 650-651 ("Janeway").

The presently claimed subject matter is directed to methods of treating inflammation by administering antibodies specific for GM-CSF, M-CSF or a combination of such antibodies and provides animal data establishing the efficacy of such treatments.

To establish obviousness, a cited reference must suggest or motivate those of ordinary skill in the art to modify its teachings or to combine its the teachings with those of other references to arrive at the claimed subject matter with a reasonable expectation of success. The cited combination of references totally fails in this regard.

The '460 patent has been extensively discussed on the record. Briefly, the '460 patent teaches a method of generating small peptide mimetics against GM-CSF (col. 2, lines 20-54), and that those peptide mimetics exhibit GM-CSF biological activity.[6] While the '460 patent suggests that these peptide mimetics can act as antagonists of GM-CSF, the only data in the '460 patent shows that some, but not all, of the peptide mimetics inhibit the proliferation of GM-CSF-dependent cell growth in cultured cells (Example 2, especially at col. 21, lines 19-64), i.e., the peptides of the '460 patent doe not predictably act as agonists

The '460 patent also suggests that the peptide mimetics with antagonist action (*i.e.*, the molecules which are considered equivalents or "copies" of GM-CSF) are anti-inflammatory agents. There is no teaching whatsoever that antibodies against GM-CSF (which molecules would never be considered as equivalents or "copies" of GM-CSF) have such activity or would

[6] The '460 patent indicates the method is generally useful for certain cytokines, including M-CSF.

be expected to have such activity. In fact, the '460 patent teaches away from the notion of using antibodies as therapeutic agents (col. 4, lines 43-46) and directs the skilled artisan to use the peptide mimetics as the anti-inflammatory agents (col. 9, lines 39-40).

According to the Examiner, the '460 patent teaches a "method of active immunization with M-CSF or GM-CSF antigen" (Office Action at Page 3, 5th paragraph) and cites Janeway for the proposition that diseases can be treated by passive or active immunization.

First, nowhere does the '460 patent suggest any mechanism of action of the peptide mimetics. Second, the '460 patent states that the useful peptide mimetics are antagonists of GM-CSF—formulated to reach GM-CSF's "site of action in the body" (col. 10, line 11)—and strongly suggesting that GM-CSF does not function by stimulating antibody production, *i.e.*, the peptide mimetics are not operating via active immunization. Third, the binding studies of Example 1 suggest that the peptide mimetics, in particular pep3, "binds to the GM-CSF-receptors" (col. 17, lines 51-52)—again not via active immunization. Fourth, peptides are poor immunogens in the absence of carriers (typically proteins such as KLH or albumin), and the '460 patent provides no teaching, suggestion or disclosure of how one might use the peptides in this regard. In fact, the need for carriers goes directly against the teaching in the '460 patent which states that peptide mimetics are used to avoid the problems associated with use of proteins as therapeutic agents (col. 4, lines 43-46). Fifth, the '460 patent teaches only that the antagonist forms of the peptide act as inflammatory agents, whereas if the peptides were acting via active immunization, the fact that a peptide was an agonist of antagonist of GM-CSF would be irrelevant. Hence, there is no basis whatsoever to assert that the '460 patent teaches active immunization and any such suggestion is simply unsupported conjecture that goes against the actual teaching of the '460 patent.

Moreover, Janeway does not ameliorate such deficiencies. The cited passage from Janeway generally discusses active and passive immunization and provides nothing more than what is common knowledge in the art. This is not specific motivation to make the claimed invention nor does it rise to a suggestion to make and use the presently claimed subject matter. In fact, the concept of active versus passive immunization brings on another level of complexity and concern for self antigens such as GM-CSF and M-CSF. Neither of the cited references address this problem—something avoided by the present invention. Accordingly, no *prima facie* obviousness exists based on the combination of the '460 patent and Janeway.

Because the '460 patent fails to provide any disclosure, teaching or suggestion that administration of antibodies specific for GM-CSF, M-CSF or both are useful to ameliorate inflammation, and in fact teaches away from such uses, the '460 patent does not render obvious the presently claimed invention, either alone or when taken with Janeway. Hence, Applicants, respectfully request that this rejection under 35 U.S.C. § 103(a) be withdrawn.

B. The Second 103(a) Rejection

Claims 29, 30 and 34 have been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by the '994 publication in view of U.S. Patent No 5,444,153 to Goss *et al.* (the '153 patent) or U.S. Patent No. 5,662,609 to Slepian *et al.* (the '609 patent). Since the '994 publication is not a valid reference against the present application, this rejection had been rendered moot and withdrawal thereof is respectfully requested.

C. The Third 103(a) Rejection

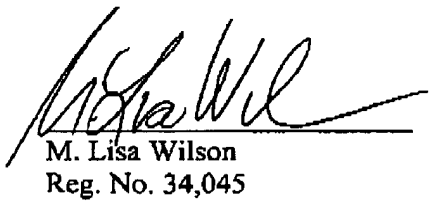
Claims 29, 30 and 34 stand rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by the '460 patent and Janeway, taken in view of the '153 patent or the '609 patent.

The '460 patent and Janeway reference have been discussed above and distinguished. Neither reference teaches, discloses or suggests that antibodies specific for GM-CSF or M-CSF have any therapeutic utility for ameliorating inflammation. Moreover, neither reference teaches the need for such antibodies. Because the secondary references (the '153 and '609 patents) relate to methods of treating inflammatory diseases in a patient by administering specific inhibitors of u-PA, they do not ameliorate the deficiencies of the primary references. Accordingly, the secondary references, either alone or in combination with the primary references, fail to render obvious the subject matter of Claims 29, 30 and 34. Applicants believe this rejection is thus overcome and respectfully request withdrawal thereof.

Conclusion

In view of the foregoing amendments and remarks, Applicants firmly believes that the examined subject matter is in condition for allowance, which action is earnestly solicited. If any issues remain outstanding after consideration of this Amendment, the Examiner is invited to contact the undersigned to expedite prosecution of this case.

Respectfully submitted,



Date: February 10, 2006

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Appendix A

All exhibits were obtained from the USPTO PAIR system Image File Wrapper (IFW) for the '994 publication.

Exhibit 1 provides the Provisional Application for Patent Cover Sheet, the title page and first two pages of the specification, the claims thereof and the abstract for Provisional B. Each page, along the left side margin, bears the PTO stamp "60270948.022301" indicating the application number and filing date of these pages to be those Provisional B, U.S. Serial No. 60/270,948, filed February 23, 2001.

Exhibit 2 provides the Petition filed on July 9, 2001 and the accompanying preliminary amendment requesting entry of a priority claim to Provisional A (U.S. serial No. 60/190,842, filed March 20, 2000).

Exhibit 3 establishes that the Petition was granted on September 5, 2001, and that the converted provisional application was accorded U.S. Serial No. 09/885,259 and a filing date of February 23, 2001.

Exhibit 4 provides the complete listing of the contents of the IFW for the '994 publication (U.S. Serial No. 09/885,259). The entries from which Exhibits 1-3 were obtained are marked on page 4 of this exhibit.

Exhibit 1

02-26-01 09885259 022301

Please type a plus sign (+) inside this box → [+]

Docket Number: A0000326L2-01CFP

PROVISIONAL APPLICATION FOR PATENT COVER SHEET (Large Entity)

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53 (c).

INVENTOR(S)/APPLICANT(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Madhav Narasimha Joseph Edwin	Devalaraja Low	2715 Windwood Dr. #62, Ann Arbor, MI 48105 921 Alpine Court, Brighton, MI 48116

☐ Additional inventors are being named on page 2 attached hereto

TITLE OF THE INVENTION (280 characters max)

INHIBITORS OF COLONY STIMULATING FACTORS

CORRESPONDENCE ADDRESS

Direct all correspondence to:

☐ Customer Number [ ] → Place Customer Number Bar Code Label here

OR

☒ Firm or Individual Name	Claude F. Purchase, Jr.				
Address	Warner-Lambert Company				
Address	2800 Plymouth Road				
City	Ann Arbor	State	Michigan	ZIP	48105
Country	USA	Telephone	734-622-1692	Fax	734-622-1553

ENCLOSED APPLICATION PARTS (check all that apply)

☒ Specification — Number of Pages: 37

☒ Drawing(s) — Number of Sheets: 21

☒ Other (specify): 30 claims on 4 pages abstract on 1 page

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (check one)

☐ A check or money order is enclosed to cover the filing fees

☒ The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 23-0455

FILING FEE AMOUNT ($): $150.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE Claude F. Purchase, Jr. DATE February 23, 2001

TYPED or PRINTED NAME Claude F. Purchase, Jr. REGISTRATION NO. (if appropriate) P-47,871

TELEPHONE 734-622-1692

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, DC 20231

[redacted]

09885259.022301

Docket Number:	A0000326L2-01CFP

PROVISIONAL APPLICATION FOR PATENT COVER SHEET (Large Entity)

INVENTOR(S)/APPLICANT(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (city and either State or Foreign Country)

Certificate of Mailing by Express Mail

I certify that this application and enclosed fee is being deposited on February 23, 2001 with the U.S. Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Cindy Malocha

Signature of Person Mailing Correspondence

Cindy Malocha

Typed or Printed Name of Person Mailing Correspondence

EK651207059US

"Express Mail" Mailing Label Number

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

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[redacted]

09825259 .022501

Express Mail No. EK651207059US

A0000326L2-01CFP

INHIBITORS OF COLONY STIMULATING FACTORS

A0000326L2-01CFP

INHIBITORS OF COLONY STIMULATING FACTORS

FIELD OF THE INVENTION

The present invention is directed to inhibitors of haematopoetic factors called colony stimulating factors and methods of treating diseases responsive to inhibition of colony stimulating factors. The present invention is also directed to assays for screening inhibitors of CSF.

BACKGROUND OF THE INVENTION

Colony stimulating factors (CSFs) stimulate the differentiation and/or proliferation of bone marrow cells. CSFs in both human and murine systems have been identified and distinguished according to their activities involving two of the three main classes of leukocytes, namely granulocytes and monocytes. For example, granulocyte-CSF (G-CSF) and macrophage-CSF (M-CSF) stimulate the in vitro formation of neutrophilic granulocyte and macrophage colonies, respectively, while granulocyte-macrophage CSF (GM-CSF) has broader activities and stimulates the formation of both macrophage, neutrophilic, and eosinophilic granulocyte colonies. These CSFs act via their respective receptors, namely G-CSFR, M-CSFR, and GM-CSFR. G-CSR is expressed on multipotential hematopoietic progenitor cells and cells of myeloid lineage, and is important for regulation of granulopoiesis.

Evidence of the role G-CSF and G-CSFR play in inflammation includes the discovery that G-CSF is frequently found elevated in serum of and at inflammatory sites in patients with infections. The undetectable normal circulating levels of G-CSF (≤10 pM) increase in inflammatory conditions to a range of from 100 to 2000 pM. Further, transgenic mice with neutrophils expressing chimeric receptors with extra-cellular G-CSFR and intra-cellular erythropoietin receptor appear to retain their normal hematopoietic function but no longer respond to chemotactic signals. Also, the chemokine interleukin-8 (IL-8) fails to induce chemotaxis of neutrophils from G-CSFR -/- mice (i.e., G-CSFR knockout mice),

suggesting a specific role for G-CSFR in neutrophil chemotaxis. However, by itself, G-CSF is a relatively weak chemoattractant.

Additionally, M-CSF, also known as colony stimulating factor-1, has been shown to increase blood and tissue macrophage numbers in several species. For example, it is known that M-CSF is produced within the joint in human rheumatoid arthritis, where it has been shown to cause severe exacerbation of the disease. This is consistent with other studies, wherein M-CSF was found to worsen the disease course of experimental disseminated candidiasis, a disease with many of the characteristics of tumor necrosis factor-mediated pathology. M-CSF was also found to stimulate secretion of urokinase plasminogen activator, which plays a role in proteolytic joint destruction. Recently, cDNA encoding the primary growth and differentiation factor for M-CSF has been isolated, sequenced and expressed, and human recombinant M-CSF is now available for experimental studies.

However, CSFs are not the only cytokines involved in inflammation. Also involved are chemokines, which are chemotactic cytokines that are released by a wide variety of cells to attract macrophages, T cells, eosinophils, basophils, and neutrophils to sites of inflammation. There are two classes of chemokines, the members of each class share an organizing primary sequence motif. Alpha chemokines such as IL-8, neutrophil-activating protein-2 (NAP-2), and melanoma growth stimulatory activity protein (MGSA) are chemotactic primarily for neutrophils, whereas beta chemokines such as RANTES (regulation-upon-activation, normal T expressed and secreted), MIP-1 alpha (macrophage inflammatory protein), MIP-1 beta, MCP-1 (monocyte chemotactic protein-1), MCP-2, and MCP-3 are chemotactic for monocytes, T-cells, eosinophils, and basophils.

Chemokines bind specific cell-surface receptors belonging to the family of G-protein-coupled seven-transmembrane-domain proteins which are termed "chemokine receptors." Chemokines and chemokine receptors such as, for example, CCR-1, CCR-2, CCR-2a, CCF-2b, CCR-3, CCR-4, CCR-5, CXCR-1, CXCR-2, CXCR-3, and CXCR-4, play a role in inflammation and autoimmune responses by attracting leukocytes, which migrate out of the microvasculature and into the extravascular space in response to chemoattractant molecules. These

CLAIMS

What is claimed is:

1. An inhibitor of a colony stimulating factor (CSF), which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising an agent which binds to a CSF, an agent which inhibits expression of a CSF, an antagonist of a colony stimulating factor receptor (CSFR), an antibody directed to a CSF or a CSFR, or an agent which inhibits activation of a CSFR, or a pharmaceutically acceptable salt thereof.

2. The inhibitor of Claim 1 wherein the CSF is a monocyte-colony stimulating factor (M-CSF).

3. The inhibitor of Claim 1 wherein the chemokine is a beta-chemokine.

4. The inhibitor of Claim 1 wherein the CSF is an M-CSF, the chemokine is monocyte chemotactic protein-1 (MCP-1), and the inhibitor is an antibody directed to an M-CSF or an antibody directed to a monocyte-colony stimulating factor receptor (M-CSFR).

5. The inhibitor of Claim 1 wherein the CSF is an M-CSF, the chemokine is MCP-1, and the inhibitor is an antagonist of an M-CSFR.

6. The inhibitor of Claim 1 wherein the CSF is a granulocyte-colony stimulating factor (G-CSF).

7. The inhibitor of Claim 1 wherein the chemokine is an alpha-chemokine.

8. The inhibitor of Claim 1 wherein the CSF is a G-CSF, the chemokine is IL-8, and the inhibitor is an antibody directed to a G-CSF or an antibody directed to a granulocyte-colony stimulating factor receptor (G-CSFR).

9. The inhibitor of Claim 1 wherein the CSF is a G-CSF, the chemokine is IL-8, and the inhibitor is an antagonist of a G-CSFR.

10. The inhibitor of Claim 1 wherein the CSF is a granulocyte macrophage-colony stimulating factor (GM-CSF).

11. A pharmaceutical composition, comprising an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient.

12. A method of treating inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising administering to a mammal, in need thereof, a therapeutically effective amount of an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, or a pharmaceutically acceptable salt thereof.

13. The method according to Claim 12 wherein the disease being treated is atherosclerosis.

14. The method according to Claim 12 wherein the disease being treated is sepsis.

15. The method according to Claim 12 wherein the disease being treated is asthma.

16. The method according to Claim 12 wherein the disease being treated is an autoimmune disease.

17. The method according to Claim 12 wherein the disease being treated is osteoporosis.

18. The method according to Claim 12 wherein the disease being treated is rheumatoid arthritis.

19. The method according to Claim 12 wherein the disease being treated is osteoarthritis.

20. A method for screening for an inhibitor of an M-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising analyzing an (M-CSF)-stimulated monocyte population using a Fluorescent Activated Cell Sorter technique.

21. The method according to Claim 20 wherein the (M-CSF)-stimulated monocyte population is analyzed in whole blood after red blood cell lysis.

22. The method according to Claim 20 wherein the screening method is a high throughput screening method.

23. The method according to Claim 20 wherein the (M-CSF)-stimulated monocyte population has also been stimulated by MCP-1.

24. The method according to Claim 23 wherein the (M-CSF)-stimulated monocyte population which has also been stimulated by MCP-1, is analyzed in whole blood after red blood cell lysis.

25. A method for screening for an inhibitor of a G-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) G-CSF to a G-CSFR in a (G-CSF)-stimulated neutrophil population.

26. The method according to Claim 25 wherein the screening method is a high throughput screening method.

27. A method for screening for an inhibitor of a GM-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) GM-CSF to a GM-CSFR in a (GM-CSF)-stimulated neutrophil population or analyzing a (GM-CSF)-stimulated monocyte population using a Fluorescent Activated Cell Sorter technique.

28. A method for screening for an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, the method comprising:

Step (a) Obtaining CSFR cDNA and corresponding (I^{125})-CSF;
Step (b) Cloning the CSFR cDNA of Step (a) into a vector;
Step (c) Stably transfecting the vector of Step (b) into a hematopoetic cell line that resembles circulating leukocytes;
Step (d) Quantitating the transfected vector of Step (c) and measuring the binding of said (I^{125})-CSF; and
Step (e) Screening agents for inhibition of CSF activity using a binding assay comprising the transfected vector of Step (c) and said (I^{125})-CSF.

29. A method for screening for an inhibitor of an M-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) M-CSF to an M-CSFR in an (M-CSF)-stimulated monocyte population.

30. The method according to Claim 29 wherein the M-CSFR is a soluble M-CSFR.

ABSTRACT

A hematopoetic factor called "colony stimulating factor" (CSF) is capable of synergizing the attracting capabilities of chemokines and of inducing the accumulation and/or activation in vitro and in vivo of key components of inflammatory responses. Various types of agents that inhibit or otherwise hinder the production, release or activity of CSF could be used therapeutically in the treatment of ischemia and other inflammatory diseases, such as autoimmune disease, and various chronic inflammatory diseases such as rheumatoid arthritis and psoriasis.

Exhibit 2

Patent Application
Attorney Docket No.PC18174A

#2

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express mail in an envelope addressed to: Hon. Commissioner of Patents and Trademarks, Washington, D.C. 20231 on this 6th day of July 2001.

(Signature of person mailing)
Seth H. Jacobs

(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION OF: Madhav N. Devalaraja and Joseph E. Low
APPLICATION NO: 60/270948 : Examiner: Not yet assigned
FILING DATE: February 23, 2001
TITLE: INHIBITORS OF COLONY STIMULATING FACTORS

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

PETITION FOR CONVERSION OF PROVISIONAL APPLICATION TO NON-PROVISIONAL APPLICATION UNDER 37 C.F.R. §1.53(c)(3)

Applicant(s) respectfully request that the present provisional application be converted to a non-provisional application pursuant to 37 C.F.R. §1.53(3)(c).

Priority of earlier filed provisional application serial no. 60/190,842, filed March 20, 2000 is claimed under 35 U.S.C. §119(e). A preliminary amendment to the present specification, adding a claim to such priority, is included herein.

Patent Application
Attorney Docket No.PC18174A

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express mail in an envelope addressed to: Hon. Commissioner of Patents and Trademarks, Washington, D.C. 20231 on this 6th day of July 2001.

By _____
(Signature of person mailing)
Seth H. Jacobs

_____
(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Madhav N. Devalaraja and Joseph E. Low :

APPLICATION SERIAL NO.: Non-provisional application converted from serial no. 60/270,948 : Examiner: Not yet assigned

FILING DATE: February 23, 2001 : Group Art Unit:

TITLE: INHIBITORS OF COLONY STIMULATING FACTORS :

Box Amendment
Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

PRELIMINARY AMENDMENT

Sirs:

Kindly amend the above referenced application as follows:

IN THE SPECIFICATION:

At page 1, line 1 of the specification, insert:

"This application claims priority of Serial No. 60/190,842, filed March 20, 2000."

Adjustment date: 08/08/2002 GDUCKETT
03/11/2002 JTIPPETT 00000001 161445 60270948
01 FC:101 710.00 CR

IN THE CLAIMS:

Add the following claims:

31 - 32. A method of treating inflammation in a mammal comprising administering to said mammal an effective amount of an m-CSF inhibitor.

31 - 33. The method of claim 32 wherein said inhibitor is an antibody.

Adjustment date: 08/08/2002 GDUCKETT
03/11/2002 JTIPPETT 00000001 161445 60270948
01 FC:101 710.00 CR

09/05/2001 JTIPPETT 00000001 161445 60270948
01 FC:122 130.00 CH
02 FC:102 480.00 CH
03 FC:103 234.00 CH

Adjustment date: 08/08/2002 GDUCKETT
09/05/2001 JTIPPETT 00000001 161445 60270948
02 FC:102 480.00 CR
03 FC:103 234.00 CR

~~33~~ 34. The method of claim 32 wherein said inflammation is associated with arthritis.~~81~~

Respectfully submitted,

Date: _____

Seth H. Jacobs
Attorney for Applicant(s)
Reg. No. 32,140

Pfizer, Inc
Patent Department, 20th Floor
235 East 42nd Street
New York, NY 10017-5755
(212) 733-3678

Exhibit 3

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www.uspto.gov

September 5, 2001

Paper # 3

Claude F. Purchase, Jr.
Warner-Lambert Company
2800 Plymouth Road
Ann Arbor MI 48105

In re Application of:	Devalaraja, et al.	:	DECISION GRANTING
Application No.:	60/270,948	:	PETITION
Filed:	February 23, 2001	:	
Attorney Docket No.:	A000026L2-01CFP	:	

This is a decision on your petition under 37 CFR 1.53(b)(1), received in the Patent and Trademark Office on July 09, 2001, to convert the above identified application to a non-provisional application under 35 U.S.C. 111 (a) and 37 CFR 1.53(b)(1).

The petition is granted.

The application will be processed in the Office of Initial Patent Examination (OIPE) as a non-provisional application under 35 U.S.C. 111(a) and 37 CFR 1.53(b)(1), including the assignment of a new non-provisional application number.

The non-provisional application serial number is **09/885,259**. The filing receipt for the non-provisional application will be mailed in due course.

Janice Tippett, Program Assistant
Office of Initial Patent Examination
(703) 308-0910

Exhibit 4

Printer Friendly
09/885,259 Inhibitors of colony stimulating factors

Image File Wrapper

This application is officially maintained in electronic form. To View: Click the desired Document Description. To Download and Print: Check the desired document(s) and click StartDownload.

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